

Amendments to the Specification:

Please replace the list of inventors on the cover page with the following

Inventors:

GLENN H. MCGALL, a citizen of Canada, residing at 750 North Shoreline,
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Please replace the cross-reference to related applications on page 1 with the following rewritten paragraph:

This is a continuation of U.S. Application No. 08/882,649, filed June 25, 1997, now U.S. Patent No. 6,344,316, which is a continuation of PCT/US97/01603, filed on January 22, 1997, designating the United States of America, which derives priority from USSN 60/010,471 filed January 23, 1996 and USSN 60/035,170, filed January 9, 1997, all of which are herein incorporated by reference for all purposes.

Please replace the paragraph beginning at page 18, line 3 with the following amended paragraph:

Figs. 14a, 14b, 14c, and 14d illustrates a ligation discrimination used in conjunction with a restriction digest of the sample nucleic acid. FIG. 14a shows the recognition site and cleavage pattern of SacI (a 6 cutter) and Hsp92II (4 cutter). FIG. 14b illustrates the effect of SacI cleavage on a (target) nucleic acid sample. FIG. 14c illustrates a 6 Mb genome (i.e., E. coli) digested with SacI and SphI generating about 1 kb genomic fragments with a 5' C. FIG. 14d illustrates the hybridization/ligation of these fragments to a generic difference screening chip and their subsequent use as probes to hybridize to the appropriate nucleic acid (Format I) or the fragments are labeled, hybridized/ligated to the [[oligonucleotide array]] oligonucleotide array and directly analyzed (Format II).

Please replace the paragraph beginning at page 18, line 12 with the following amended paragraph:

Figs. 15a, 15b, 15c, 15d, and 15e illustrate the analysis of [[differential display]] differential display DNA fragments on a generic difference [[screening]] screening array. Fig. 15a shows first strand cDNA synthesis (SEQ ID NO:7) by reverse [[transcription]] transcription of poly(a) mRNA using an anchored poly(T) primer (SEQ ID NO:8). Fig. 15b illustrates upstream primers for PCR reaction containing an engineered [[restriction site]] restriction site and degenerate bases (N=A,G,C,T) at the 3' end. Fig. 15c shows randomly primed PCR of first strand cDNA. Fig. 15d shows [[restriction digest]] reaction digest of PCR products, and Fig. 15e shows sorting of PCR products on a generic [[ligation array]] ligation array by their [[5' end]] 5' end.

Please replace the paragraph beginning at page 19, line 4 with the following amended paragraph:

Fig. 19 provides a schematic illustration of pos-hybridization end labeling (SEQ ID NO:9) on a high density oligonucleotide array.

Please replace the paragraph beginning at page 19, line 10 with the following amended paragraph:

Fig. 22 illustrates oligo dT labeling on a high density oligonucleotide array (SEQ ID NOS:10 and 11).

Please replace the paragraph beginning at page 19, line 15 with the following amended paragraph:

Fig. 24. illustrates resequencing of a target DNA molecule with a set of generic n-mer tiling probes (target sequence is SEQ ID NO:12).

Please replace the paragraph beginning at page 19, line 26 with the following amended paragraph:

Fig. 32 illustrates mutations found in an HIV PCR target (B) using a generic ligation GeneChipTM and induced difference analysis (SEQ ID NOS:13-32 respectively).

Please replace the paragraph beginning at page 57, line 12 with the following amended paragraph:

If any probe failed one of these criteria (1-8), the probe was not a member of the subset of probes placed on the chip. For example, if a hypothetical probe was 5'-AGCTTTTTTCATGCATCTAT-3' (SEQ ID NO:1) the probe would not be synthesized on the chip because it has a run of four or more bases (*i.e.*, run of six).

Please replace the paragraph beginning at page 58, line 28 with the following amended paragraph:

The simplest pruning method is to line up a proposed probe with all known genes for the organism being monitored, then count the number of matching bases. For example, given a probe (SEQ ID NO:2) to gene 1 of an organism and gene 2 (SEQ ID NO:3) of an organism as follows:

probe from gene 1: aagcgcgatcgattatgctc

gene 2:	atctc	g	g	a	t	c	g	a	t

has 8 matching bases in this alignment, but 20 matching bases in the following alignment:

probe from gene 1:	a	a	g	c	g	c	a	t	c	g	a	t	c	g	a	t	a	t	g	c	t	c
gene 2:	a	t	c	t	c	g	a	t	c	g	a	t	c	g	a	t	a	a	g	c	g	c

Please replace the paragraph beginning at page 81, line 1 with the following amended paragraph:

The principle behind differential display is to ~~[[generat]]~~ generate a set of randomly primed amplification (*e.g.*, PCR) fragments from a first strand cDNA population transcribed from RNA using anchor primers of the form:

(T)_nVA, (T)_nVG, (T)_nVC, and (T)_nVT (SEQ ID NO:4)

in which V is A, G, or C, and n ranges from about 6 to about 30, preferably from about 8 to about 20 and more preferably about 10 to about 16 with n=14 being most preferred. Depending on what random primer and anchoring primer [and anchoring proimer] is chosen, different sets of cDNA transcripts are represented in a particular nucleic acid fragment set. These amplification fragments are analyzed by sorting the fragments on a generic screening oligonucleotide array where they hybridize based on the sequence at the 5' end of the [[fragment]] fragment.

Please replace the paragraph beginning at page 139, line 11 with the following amended paragraph:

The following 5' sequence (SEQ ID NO:5) has worked well (with 19-21 gene-specific bases added at the 3' end).

5'-GAATTGTAATACGACTCACTATAGGGAGG-[+19-21 gene specific bases]-3'

The 5' end consists of:

- a) six 5' flanking bases of your choice – not part of the promoter sequence, but necessary for maximum IVT efficiency.
- b) 17 bases of the core T7 RNA polymerase promoter sequence
- c) 1st 6 bases transcribed (sequence of +1 to +6 can affect efficiency)

The other PCR primer would then contain the T3 RNA polymerase promoter sequence at the 5' end. The following sequence (SEQ ID NO:6) has worked well:

5'-AGATGCAATTAACCCTCACTAAAGGGAGA-(+19-21 gene-specific bases)-3'

The 5' end consists of:

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- a) six 5' flanking bases (sequence can vary from this example)
- b) 17 bases of core T3 RNA Polymerase promoter sequence
- c) +1 to +6 transcribed bases